10

The Problems of Therapeuti

Address delivered before the Section on Therapeutics and Pharmacology
at the International Congress of Arts and Science
at St. Louis, Sept. 24, 1904

◆

By SIR LAUDER BRUNTON, M.D., D.Sc., LL.D.

Consulting Physician to St. Bartholomew's Hospital, London

◆

REPRINTED FROM THE THERAPEUTIC GAZETTE, OCTOBER AND NOVEMBER, 1

◆

ROYAL COLLEGE OF SURGEONS OF ENGLAND
-7 APR 11
LIBRARY

DETROIT, MICH.
E. G. SWIFT, PUBLISHER
1904

ROYAL COLLEGE OF SURGEONS OF ENGLAND LIBRARY

THE PROBLEMS OF THERAPEUTICS.

By Sir Lauder Brunton, M.D., D.Sc., LL.D., F.R.S.

Mr. President, Ladies and Gentlemen—The subject of my lecture to-day is "The Problems of Therapeutics." My audience is a select one of persons interested in science and art. But science in these days has branched out so widely that it is impossible for any single person to be acquainted with every department of it, and the terms used by a zoölogist may be unintelligible to a mathematician, or *vice versa*. There are many here whose researches have led them far into abstruse departments of science, and if they were speaking I should gladly welcome a few introductory words from them on the very rudiments of their science in order to help me to understand a disquisition on the more advanced parts of their subjects.

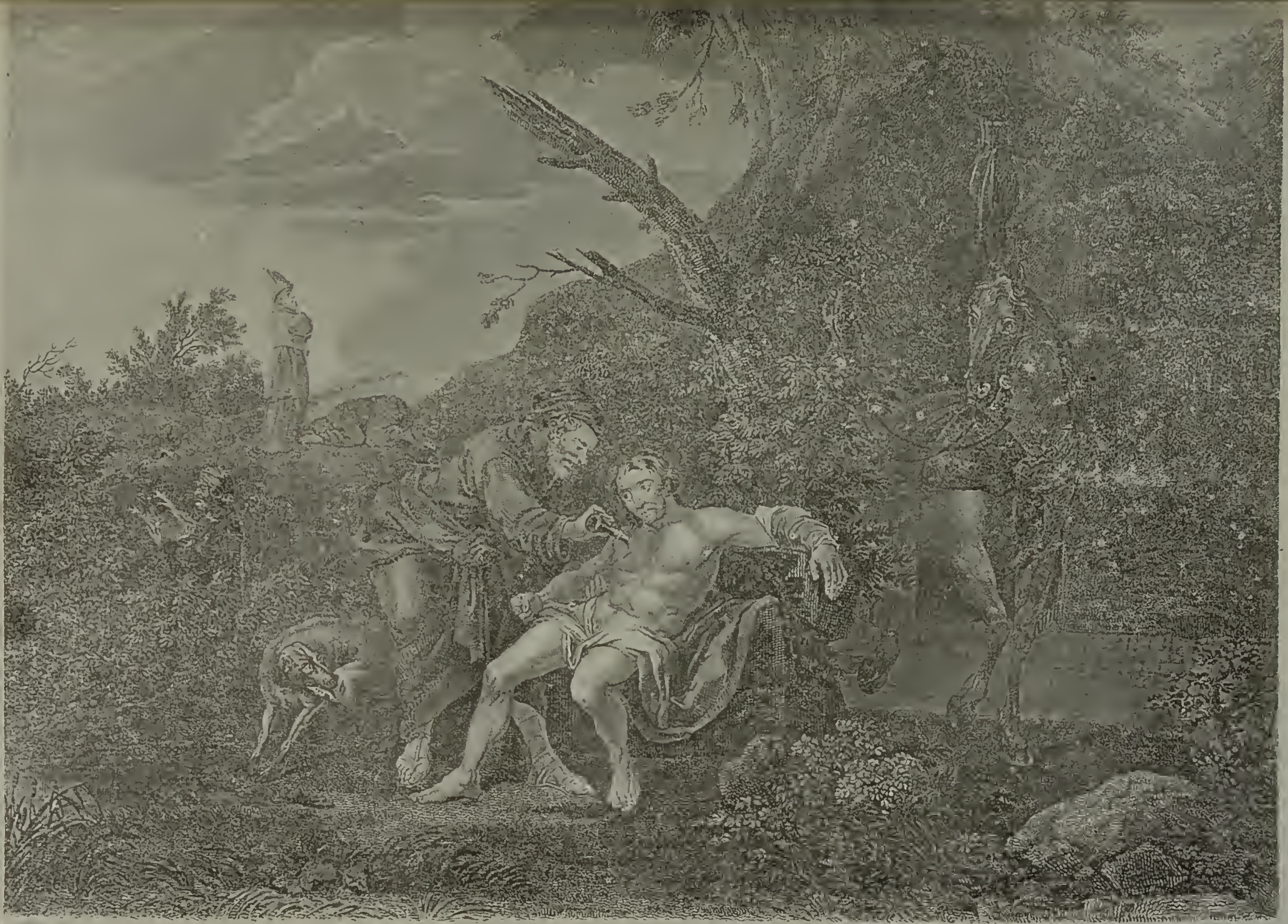
Judging others by myself I think they may be glad if I do the same, and I must beg the indulgence of those who are acquainted with medical science if this lecture should seem to be unnecessarily rudimentary. By therapeutics we mean the methods of healing.

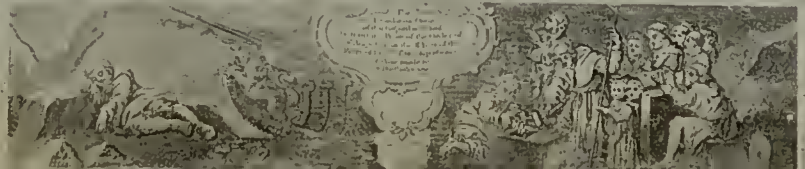
In the great staircase of St. Bartholomew's Hospital in London there is a large picture by William Hogarth representing The Good Samaritan. The poor traveler is seated on the ground, the good Samaritan is pouring oil and wine into his wounds, while close at hand is a dog busily engaged in licking a cut which he has received in the fray. Both dog and man are engaged in solving as far as they can two of the primary problems of therapeutics, viz.: (1) How to relieve pain, and (2) how to restore health. For disease is want of ease, and "health" is only one form of the word "whole," by which we mean that a thing is entire and neither cut, broken, nor cracked. The closure of wounds is one form of restoring "wholeness" or "health" to the body, but it is by no means the only one, for the vital organs lie below the surface and it is with disturbances of their functions, even more than with external wounds, that therapeutics, or the science and art of healing, is chiefly occupied. As exemplified in the dog or in the Good Samaritan therapeutics is simply an art. Certain things are done because they have been found to do good before and so they are repeated again and again, but neither the dog nor the Good Samaritan understand the reason why their procedure is useful. It is only when we learn the reason why, that an art becomes converted into a science. Therapeutics in its primitive form is one of the simplest of all the arts, and is practiced by animals as well as by man, but as a science it is one of the most complex and most difficult of all, because it requires a knowledge of the functions of the body in health, or physiology, of their changes in disease or pathology, of the action of drugs upon the body or pharmacology, and of chemistry, physics and other sciences on which physiology, pathology and pharmacology are based. Finally it requires the practical power of recognizing from the symptoms (in any individual case) the nature of the pathological changes present and the ability to apply the right methods of treatment in order to counteract these changes and heal the patient. It is evident that such complex knowledge as this must be very difficult of attainment, yet nevertheless the change of therapeutics from an art into a science is progressing with considerable rapidity. In a text-book on the subject which I published eleven years ago, I mentioned the use of quinine in ague as the best example of the art of therapeutics whereby we could cure a disease of which we did not know the nature, by a remedy whose curative action we did not understand. Since that time, however, we have learned that ague depends upon the presence of a foreign organism in the body and that the benefits obtained from quinine are due to its poisonous action upon this intruder. This malarial parasite is only one of the many minute organisms which mar or destroy the health of the human body. Minute organisms or microbes are most useful in their proper place, and without them the world would be uninhabitable, because they are the natural scavengers which produce putrefaction in dead plants and animals and thus bring about their return to dust, fitting them for new life instead of allowing them to encumber the ground. But not content with this function some of them proceed to invade living beings, attacking not only the weak but even the strong, and by growing and multiplying within them weaken or destroy their hosts.

One of the great problems of therapeutics then is to defend the body from attacks of microbes. This may be done either (*a*) by weakening or destroying the microbes themselves, or (*b*) by increasing the power of the organism to resist them.

It is convenient to speak of the body as a whole when we are discussing its invasion by microbes, but we must not forget that the body, like a country, is composed of many parts. The interests of the different parts are by no means identical, and while they generally act together for the common good they may not always do so, and either by their sluggishness and inaction or by their mischievous activity they may do harm instead of good to the body as a whole. What is requisite for health is a harmonious action of all the different parts of the body, or as St. Paul very well puts it, "And thus all the body framed and knit together through that which every joint supplieth, according to the working in due measure of each several part, maketh the increase of the body unto the building up of itself" (Ephes. 4, 16, revised vers.), so "that there should be no schism in the body and that the members should have the same care one for another." No doubt in their long wanderings together Luke, the beloved physician, discussed physiology largely to Paul, and his expression is so good that I have quoted it now. Just as the people of a country is composed of individuals, so the body is composed of numerous cells. The whole class of microbes consists of isolated cells which are like a nomad population, each individual complete in himself, and ready to form a swarm for attack and invasion. The cells which compose the body, on the contrary, are mostly fixed, and differ from each other in structure and function, but ought all to act together for the common good. Each cell lives in the fluid which surrounds it, blood or tissue juice, from which it takes what it needs for its own nutriment and pours back the products of its tissue activity, which may be partly waste and partly manufactured products of the utmost utility.

In order to have a complete comprehension of therapeutic problems it is necessary that we should know something about the life of the cell, because the life of the whole body depends upon that of the cells which compose it, and the cure of disease and preservation of life depend on our power to influence cell life. The processes of life are to a certain extent the same in the human body as a whole, in the cells which compose it, and in the smallest living organisms, or microbes as they are termed. They all digest and assimilate food, they all breathe, and they all excrete waste products. A knowledge of the processes of life in man helps us to understand them in low organisms, and *vice versa*. The use of pepsin and pancreatin in indigestion is so common that almost everybody knows that these substances have the power of dissolving meat and that pancreatin converts starch into sugar. Everybody knows that these are got from the stomach and pancreas of animals, and that it is by similar substances formed in our own digestive canal that we are able to dissolve the food we eat and render it fit for absorption. It has recently been found that pancreatic juice, as poured out by the gland which secretes it, is very slightly active, but it is made active by another ferment secreted





THE GOOD SAMARITAN.

Painted by William Hogarth.

from the intestine which is called enterokinase. The pancreatic juice contains several ferments; that which acts upon meat is called trypsine and in its inactive state it is called trypsogen. The action of the enterokinase on the trypsogen may be compared to that of a man who opens the blade of a knife and renders an instrument previously inactive very active indeed. If trypsine were absorbed into the blood unchanged it might digest the tissues themselves, and it must be rendered again inactive. This seems to be effected by certain substances present in the blood, which have a so-called "anti" action upon the ferments and render them again inactive. But though the digestive ferments might do harm if present in the blood in an active form and in large quantity, yet it is probable that all the cells of the body digest the food which is brought to them by the blood and tissue juices and break up this food for their own use by ferments which they contain themselves. Thirty years ago I advanced this view and supported it by the fact that I was able to extract from muscle a substance which decomposed sugar. This observation received but very little attention at the time, but recently German literature is full of papers which support my views and confirm my results, although their writers appear to be in ignorance of my work. Fifteen years ago, along with Dr. Macfadyen, I showed that bacteria not only excrete ferments by which the soil in which they are growing is digested, but that they are able to modify these ferments in accordance with the soil so as to digest either proteid matter or sugar. Curiously enough, within the last few years the pancreas in animals has been shown by Professor Pawlow to have similar powers. No individual microbe has received so much attention as the yeast plant, and no poison which is formed by any of them has done so much harm as the toxin or poisonous substance produced by yeast, for this toxin is alcohol, whose poisonous action has given rise to the general term intoxication. The yeast plant, when grown in sugar, excretes into it a ferment, invertase, which splits up cane sugar or saccharose into two other sugars, dextrose and levulose. The yeast plant may be separated from the solution of sugar by filtration, but the ferment which is already excreted will remain in the filtrate and may still continue to act on the sugar just as pepsin may dissolve a piece of meat in a jar although the pig which produced it is dead and gone. But no alcohol will be formed by this excreted ferment. Alcohol is produced by something contained within in the body of the yeast itself, and its production was formerly supposed to be due to so-called vital action. It has now, I think, been proved that alcohol is produced by the action of a ferment which is contained within the body of the yeast cell and is not excreted from it so long as the cell is intact, but only passes out after the cells have been crushed into fragments. Whilst the cell is alive and intact it absorbs the sugar into its interior, breaks it up there, and forms the alcohol or toxin. Other microbes in like manner absorb nutriment and may excrete toxins, though the nutriment and toxins of bacilli in general differ from those of yeast.

We see therefore that:

1. Cells excrete ferments.
2. They excrete poisons formed within their bodies; and
3. When they are broken up they may liberate other ferments.

The ferments excreted by microbes apparently prepare the substance in, or on, which they are growing for assimilation, and the ferments within the cell body decompose it further in the process of growth. To make this clearer I may perhaps be allowed to use a very crude illustration, and compare the ferment which is poured out by a bacillus to the saliva which is said to be poured out by the boa constrictor on its victim to facilitate deglutition, while the ferments within the microbe may be likened to those within the serpent's stomach by which actual assimilation is effected. It is probable that all cells, whether they be wandering microbes or cells coördinated in an organism, prepare and assimilate their nutriment by means of ferments; and as I have already mentioned, not only have bacilli the power of excreting ferments but apparently they are able to adapt the ferment which they excrete to the soil in which they are growing, and in much the same way as the pancreas in animals modifies the ferments it forms according to the food which it is required to digest.

Not only is digestion carried on in the stomach and intestines by the ferments which are now so well known even to the general public, pepsin, pancreatin, etc., which dissolve the ingested food so that it is readily absorbed into the circulation and carried to every part of the body, but the cells which compose the various parts of the body, muscles, nerves and glands, probably carry on the functions of their life by means of ferments also. By means of these they alter and assimilate the various substances which are brought to them by the blood and juices of the body, and after having supplied their own wants they throw into the circulation the altered residue of their pabulum as well as the substances which they have themselves formed in their processes of growth. In fact they probably repeat what we have already seen to occur with yeast, which not only alters the sugar in which it grows by a ferment which it excretes, but also produces carbonic acid and alcohol by means of a ferment which remains within the yeast cells so long as these are intact, and only becomes liberated when these cells are broken up.

An excessive quantity of their own products is usually injurious to cells, and too much alcohol will stop the growth of yeast. At the same time these products are frequently very nutritious for cells of a different sort, and alcohol furnishes a most suitable pabulum for the organisms which produce vinegar. Vinegar in its turn is toxic to the microbe which produces it, but serves again as a soil for another which gives rise to a viscous fermentation. By the successive action of these ferments a solution of sugar may produce, first alcohol, secondly vinegar, and thirdly ropy mucus. In this particular series each microbe produces a substance injurious to itself but useful to its successor. This is however not always the case, because a cell may produce a substance not only injurious to itself but injurious to other cells, and alcohol in large quantity not only kills the cells of yeast but kills other cells as well. Similar conditions occur within living organisms where the cells composing the different parts are connected together and pass on the products of their life from one cell to another by means of the circulation of blood and tissue juices. The secretions of one part may be, and indeed generally are, useful to other parts of the organism, and so long as no part sins either by deficiency or excessive action the whole organism maintains a condition of health. But this is not always the case, and health may be destroyed by (*a*) excessive, (*b*) defective or (*c*) perverted action of one or more of the parts composing the body.

But health is even more frequently destroyed by the invasions of organisms from without. When these organisms fall upon an open wound they tend to grow and multiply rapidly, they secrete ferments and form poisons which enable them to destroy the tissues upon which they have fallen, and then finding their way into the circulation and being carried to all parts of the body they kill the animal which they have attacked.

One of the great problems of therapeutics then is to discover how best to defend ourselves against the attacks of microbes. In Hogarth's picture we see two methods by which this is done. The dog licks the wound it has received and thus removes from it any pathogenic organisms which may have lighted upon it. By insuring their absence it renders the wound *aseptic,* and asepsis, which is another word for excessive cleanliness, insuring the absence of organisms, is one of the great measures by which the triumphs of modern surgery have been achieved. The treatment applied by the Good Samaritan to the wounds of the traveler is somewhat different, for he pours in wine, the alcohol of which may hinder the germination of any microbes on the wound and thus prevent them from producing sepsis. This method, which in the hands of Lister has revolutionized surgery, is termed *antiseptic* as distinguished from the *aseptic* method used by the dog. There is no doubt that the aseptic method has distinct advantages over the antiseptic method as applied to wounds because any substance which injures or destroys microbes will likewise injure the living cells of that part of the body to which it is applied. For this reason the aseptic method can only be employed to a very limited extent against microbes that have already entered the interior of the body, although it may sometimes be used, as for example in the treatment of dysentery, where repeated doses of saline purgative are now given so as to wash out from the intestinal canal the microbes which give rise to the disease, and even in ordinary diarrhea, where a purgative is employed to get rid of both the microbes and the poisons they have formed. More commonly, however, we have to depend on antiseptic methods either entirely, or as an adjunct to asepsis, and a study of the action of various chemical substances on microbes has led to the introduction of a whole series of antiseptics and indeed to their actual synthetic formation, the problem to be solved being, how to produce a body which shall destroy the microbes most efficiently and at the same time shall have the least injurious action upon the body of the animal invaded. Nor is it only inside the body that the action of antiseptics is desired. The search for preservatives for milk, meat, fish, vegetables and fruit which shall be at the same time efficient and innocuous is one constantly going on at present. Asepsis is one of nature's methods of defense. When irritating substances get into the eye a flow of tears occurs to wash them away, from the nose and respiratory passages they are ejected by sneezing or by cough, and from the stomach or intestines they are removed by the vomiting and purging to which they themselves give rise. Even in the addition of preservatives in milk we seem to be following the example of nature, because Andeer has found resorcin, which is an antiseptic, in the fresh milk of cows. As Metschnikoff has shown, another method adopted by nature of removing and destroying infective microbes is to bring down upon them a host of white blood-corpuscles or leucocytes which swallow up and destroy them. The more leucocytes that the organism can bring to bear upon the intruders the better chance it has of overcoming them. One problem therefore in therapeutics is to increase leucocytosis. At present we have comparatively few drugs that possess this power, cinnamate of soda being perhaps the most active, but one of the problems to be solved is to find other substances which will do this to a greater extent than at present. The microbes on their part are ready to attack the leucocytes and fixed cells by means of toxic secretions or toxins, and another of the defensive mechanisms which the organism adopts is to form *antitoxins,* as the antidotes to these toxins are generally termed. Some of these defensive bodies or alexins actually destroy the invading microbes themselves while others simply neutralize the poison or toxins they have formed. The nature of such defensive substances has been examined by Ehrlich, to whom we owe much of our knowledge concerning them. It is very complicated, and we do not yet know the precise mode of production of these antitoxins, but it is a curious fact that in many plants we find two poisons which are antagonistic in their action and which are to a certain extent antidotal to one another. Thus in jaborandi we have two alkaloids, one of which, pilocarpine, stimulates secretion enormously, and the other, jaborine, which paralyzes secretion, so that an extract of the jaborandi plant containing them in proper proportion might appear inactive although it contained both alkaloids in considerable amount. The same is the case with poisonous mushrooms, which contain a poisonous alkaloid, muscarin, which produces severe irritation of the intestine, and an atropine-like substance which antagonizes it. Opium likewise contains alkaloids having very different actions, some being almost purely narcotic and others purely convulsant. The animal body seems to have a wonderful power of accommodating itself to the action of many poisons, and this is very marked indeed in the case of opium. Many persons who begin with a small dose increase this gradually to an enormous extent, so that they are able to take with impunity many times the ordinary lethal dose. The organism has a certain power of storing up antidotal substances within itself, and Dr. Cash and I were able, by feeding animals with potash, to render them less susceptible to the poisonous action of barium; but except in the case of arsenic the organism seems to have but little power of becoming accustomed to inorganic poisons. It is different, however, in the case of organic poisons, as shown by the resistance to the action of alcohol acquired by habitual topers and to morphine by habitual opium eaters. A similar resistance may be acquired to snake venom and to the toxins produced by microbes, and here it does not seem to be merely that the cells of the organism become accustomed to the poison, but that the organism forms an antidote, not only in sufficient quantity to neutralize the poison which is introduced, but actually in such superabundance that serum separated from the blood of an animal which has become immune to the action of snake venom or of toxins will neutralize the effect of the venom or toxins in another animal. So great is this power that Sir T. R. Fraser has found by inoculating an animal with gradually increasing doses that it may at length completely resist the action of fifty times the ordinary lethal dose of snake vemon; and in an experiment of Monsieur Calmette I have seen an animal which had received the serum from such an immunized animal remain healthy and well, although another one which was inoculated at the same time and with the same dose of snake venom was dying from the effect of the poison.

When horses are inoculated with successively increasing doses of the toxin of diphtheria, their blood acquires a high antitoxic power, and the use of the serum of such blood injected into patients suffering from diphtheria has robbed this disease to a great extent of its awful power. Hydrophobia is another disease which has been to a great extent deprived of its terrors by Pasteur's method of treatment. This differs in its plan from that used in diphtheria. In diphtheria the bacilli probably form a ferment which produces a deadly poison by exercising its digestive powers on the material it finds in the body. This poison is neutralized by the antidotal serum which is formed in a horse and is injected into the patient. In hydrophobia we have not been able to isolate the virus, but from its mode of action we suppose it to be a minute organism. This virus takes a long time to act in man, sometimes three weeks but usually six weeks, but when cultivated successively in rabbits it becomes very virulent indeed and acts much more quickly. It apparently finds its chief seat in the spinal cord. When the cord is exposed to air the virus gradually becomes weakened, and by injecting with an extract of very weak cord on the first day and with a stronger extract on each succeeding day the human body becomes accustomed to the virus and forms its own antitoxins. Thus by the time that the poison inoculated by the original bite of the rabid animal has time to develop its action the person has become immune.

One of the most important problems of therapeutics, therefore, is to render the human body immune against pathogenic microbes, against the ferments they form and the toxins they produce. The two examples I have already given show how the toxins and possibly the ferments may be rendered innocuous by injecting antidotal sera and thus producing what is called *"passive immunity,"* or by exciting the body to form antidotal substances itself and thus produce what is called *"active immunity."* Both these methods have been used and are being used in regard to other diseases, especially in those produced by micrococci of various sorts which give rise to suppuration and inflammations. One great difficulty in the way, however, is that the antidotal serum produced by one coccus is not always efficient against the disease produced by another, and so much is this the case that it would almost seem as if an antidota serum would require to be made for each particular patient. Nor are the sera altogether innocuous themselves, because their injection may be followed not only by annoying rashes on the skin but by general swelling of the body like that from advanced kidney disease, or by painfu swelling of the joints almost like rheumatic fever. One of the problems o therapeutics therefore is to obtain anticoccic sera which will not produce an unpleasant or dangerous symptoms. An other is to confer on the tissues of th body the power of resisting or destroyin microbes, their ferments and their toxins, and thus protecting themselves, or in other words acquiring immunity against the diseases which the microbes would produce. In considering this question it may help us if we remember that the products of our own digestion are poisonous and if the albumoses and peptones formed by the digestion of a beefsteak in the stomach were injected directly into a man's veins they would kill him, whereas when changed by the cells of the intestine and liver in the process of absorption they nourish and strengthen him.

The complexity of toxins and antitoxins is easily understood when we consider that they are probably all formed by the splitting up of albuminous molecules, and thus vary enormously, just as the splinters of a broken glass vary in size, shape and in power to puncture or cut.

In my address at Moscow in 1897 I ventured to formulate the idea that "immunity, natural or acquired, is nothing nore than an extension to the cells of the issues generally of a power which is contantly exercised during digestion by hose of the intestine and liver."

When microbes were just beginning to e recognized as the cause of infective disase too much importance was attached to he mechanical effects which they might roduce in the blood-vessels and tissues. s their mode of action became better nown, this view was to a great extent iven up, but though the small vegetable nicrobes, bacilli and cocci, have little injuious mechanical action, this is not the case vith some minute organisms belonging to he animal kingdom, and such organisms f late years have become more and more ecognized as causes of diseases. In elehantiasis the lymph channels become locked by the ova of a small worm which habits the blood, and thus the enormous welling characteristic of the disease is roduced. Within the last few years that readful scourge of tropical countries, ialaria, has been discovered to be due to n animal parasite, and Manson and Ross ave shown that the source of infection the mosquito. By destroying mosquies or preventing their multiplication the sease can be to a great extent prevented. it we are still dependent upon bark, quinine, and arsenic as remedies to destroy the parasite and cure the disease. These are not invariably successful, and we are still in want of medicines which shall infallibly destroy the parasite. The same is the case with other maladies where the infective microbe is of animal origin as in sleeping sickness, which is now attributed to a minute worm in the blood, or of vegetable origin as in ulcerative endocarditis, or of uncertain origin as in yellow fever. But all these diseases excite much less attention than that which is perhaps more dreaded than any other in temperate climates, namely cancer. We do not as yet know the pathology of this disease. It has been shown that in it the cells of the affected part multiply and grow in a different manner from that of ordinary tissues. They assume a reproductive type and grow independently of the tissues of the body in which they are situated. We know that portions of carcinomatous growths may be carried by the blood stream from one part of the body to another, where they may act as new foci, but they can be transplanted with difficulty if at all from one animal to another, and thus it is evident that although their reproductive power is great their vitality is feeble. Therefore what one may hope for is, that although all the drugs hitherto tried have been powerless to prevent the life and growth of such tumors, yet something may yet be found which will attack and destroy them and nevertheless leave uninjured the healthy tissues by which they are surrounded. Lupus and rodent ulcer situated on the surface of the body have been successfully treated by the x-rays and ultraviolet rays. These have little effect on deep seated cancer. My friend Sir William Ramsay thinks however that the emanations from radium which are to a certain extent soluble in water might be administered with a view of destroying internal cancer, more especially as he has already found that they seem to have no injurious action when given to healthy animals.

In the case of cancer it is certain that groups of cells take on a life of their own and live independently of the wants of the organism as a whole, and in some other diseases we find that entire organs become too active and thus injure the health of the whole body. One of the best examples of this is the thyroid gland, which, when hypertrophied, produces, through the secretion which it pours into the blood, a curious set of nervous symptoms, dilatation of the vessels, palpitation of the heart, tremor, restlessness, excitement and rise of temperature. In the disease known as Graves's disease these symptoms exist and may possibly be aggravated by the condition of the nervous system which causes the characteristic protrusion of the eyeballs and the swelling of the thyroid itself. But that most of the symptoms are really due to the thyroid secretion is shown by the fact that they may all be observed after excessive administration of dried thyroid gland. Here we have a toxin formed within the body by the overaction of one of its parts, and at present we have no satisfactory antitoxin by which we can remove the symptoms, although suprarenal gland has an action somewhat antagonistic to that of the thyroid, and this gland or its extract when administered internally in cases of exophthalmic goitre sometimes appears to be beneficial. The case is very different however when, instead of being excessive, the action of the thyroid is deficient. When this occurs in adults the circulation becomes poor, the skin cold, the movements of the body and the action of the mind slow, the aspect becomes dull and heavy and the features puffy and swollen. When thyroid gland or its extract is given all these symptoms disappear, and the patient becomes healthy for the time and usually remains so as long as the administration is continued. When deficiency of the thyroid occurs in childhood the effect of treatment is still more manifest, for the child thus affected becomes stunted both in body and mind, is dwarfish, feeble, and idiotic. Under the administration of thyroid it grows rapidly and becomes strong and intelligent, and indeed develops into a perfectly normal person. The cure effected by thyroid in such cretins is one of the most marvelous achievements of therapeutics, and many attempts have been made with portions of other organs or extracts of them to supply material which is supposed to be absent in various diseases.

The first instance of this method of treatment, or opotherapy as it is called, was I believe my employment of raw meat thirty years ago to supply the body with a ferment to use up sugar in diabetes.* The method was reintroduced by Brown-Séquard with more success, but it was not until the use of thyroid gland and its extract that the potentialities of the method became acknowledged. It is more than eighteen hundred years since the question was asked "Who can add a cubit to his stature?" and all this time we have remained ignorant of any plan by which we could add a single inch to a child's stature. Yet it now seems possible that by the use of thyroid gland and pituitary body, children who would be otherwise stunted may grow not only to the normal size but even above it.

So long, however, as we do not know the chemical nature of the substances which exercise such an extraordinary effect upon tissue change we shall not be able to deal with them satisfactorily. We can now, in a way that was formerly impossible, regulate the temperature in fever. The clinical thermometer not only shows us the extent to which fever is present, but it enables us to stop the application of our remedies in time so as not to reduce the temperature to too great an extent. Cold water, ice and diaphoretics were formerly the only antipyretic remedies, next salicin and quinine were introduced, then salicylic acid was made synthetically, and being cheap was used extensively, and within the last thirty years an increased knowledge of chemica methods and of the relationship between chemical constitution and physiologica action has enabled numerous synthetic products to be formed, some of which may be more useful in certain cases than the original salicylate of soda.

A great many of these substances pri marily intended to reduce the temperature have turned out to have a still more im portant action, namely, the relief of pain. There is no doubt that pain is useful as a warning against conditions which tend to destroy the organism, and leads us to shun or remove these conditions to th great advantage of our health, but it i

---

**British Medical Journal*, 1873.

not always possible to do this, and pain *per se* is one of the greatest evils that poor humanity has to bear. The introduction of antiseptics has completely revolutionized the art of surgery because it allows operations to be done with almost certain success which would in former days have almost inevitably proved fatal from unconscious contamination of the wound by disease germs. But the greatest triumphs of surgery have only been rendered possible by the discovery of anesthetics. Previous to the work of Long, Jackson, Wells, Warren and Simpson rapidity of operation was everything—careful but long continued manipulation was impossible, because the long continued pain of the operation would inevitably have killed the patient. Even the minor pains of neuralgia, neuritis and headache, though not dangerous to life, are most distressing to the sufferer. Formerly there was almost no drug to relieve these excepting opium, while now we have phenacetin, antipyrin, phenalgin, and a host of others, and chemists are daily at work preparing new and perhaps even better pain killers.

Hardly, if at all, less distressing than pain is sleeplessness, and here again our powers of helping the patient have been enormously increased of late years. When I was a student almost the only hypnotics used were opium, henbane, and Indian hemp. The latter two were very unsatisfactory, and practically one pinned one's faith on opium, which had to be combined with tartar emetic in cases of fever. Then came the introduction by Liebreich of chloral, which was not only a great boon in itself, but marked an epoch as one of the first instances of rational therapeutics, the application of a certain drug in disease because of its pharmacological action. Now we have any number of hypnotics, some of which are useful because they act on the nervous system itself and produce sleep without depressing the heart, and can thus be given where the circulation is already weak, while others, like chloral, not only act on the cerebrum, but lessen the force of the circulation, and by thus diminishing the flow of blood through the brain assist it to rest and aid the onset of sleep. Formerly, when the circulation was too active, the chief depressants were mercurial and other powerful purgative medicines, bleeding, tartar emetic, vegetarian diet or partial starvation. Although these means may still be employed with advantage in proper cases, yet we have in addition a new set of remedies, viz., vasodilators, including nitrites, nitrates, and possibly a good many substances which dilate the vessels and lower the tension in the arteries, a tension which may be dangerous on the one side to an enfeebled heart, and on the other to an atheromatous artery in the brain.

When the heart is failing we have a series of cardiac tonics and stimulants. Foremost amongst these, perhaps, may be put strychnine, the action of which on the heart was practically unknown when I was a student, and perhaps now it is hardly sufficiently recognized. At the time of which I speak, digitalis was looked upon as a cardiac depressant, and almost the only cardiac stimulant that was known was alcohol. Now digitalis, strophanthus and a number of others are regularly used as cardiac tonics, and their power of contracting the vessels is also sometimes useful in removing dropsy; when this action is likely to be harmful to a weak heart it may be lessened by the simultaneous administration of vascular dilators. We still, however, want drugs which will act only on the heart, or only on the vessels. We require medicines which will diminish the cardiac action and dilate the vessels for use in high tension, such as so often occurs in gout, and we need drugs which will make the heart beat more forcibly while they cause the vessels to contract and raise the tension in cases of debility.

But prevention is better than cure, and if by modifying tissue change we can obviate the high tension and hypertrophy of the heart which so frequently lead to apoplexy, or the atheromatous condition of the vessels which leads to senile degeneration of the brain or premature old age, we shall lessen the necessity for either cardiac tonics or vascular dilators. Some authorities claim that they can do this by vegetarian diet, limited in quantity as well as quality, while others would treat it by a diet almost entirely of meat, with liberal potations of hot water.

The subject of diet is one regarding

which the most contradictory opinions prevail, and there is a sad want of precise knowledge upon which to base dietetic rules. We may hope, however, that the investigation at present being conducted by Professor Atwater under the United States government, combined with that which is being carried on under the auspices of the Carnegie Trustees, will furnish the information we need.

Time will not allow me to do more than mention the rest—aerotherapeutics, balneotherapeutics, and hydrotherapeutics; the rest-cure, which is associated with the name of one of America's most brilliant and versatile sons, Weir Mitchell; massage and movements, which Ling and his pupils both in Sweden and elsewhere have done so much to elaborate, and which when rightly used may be so beneficial, and wrongly used so harmful.

For all these branches of therapeutics we require a more exact knowledge of their action and the rules for employing them, so that even those who have made no special study of them may employ them rightly in all diseases in which they may possibly be of service.

Another method of cure consists in eliminating waste products from the body by rendering them more soluble, and thus in gout while limiting the amount of water drunk would give lithia, piperazine, piperidine and other substances which increase the solubility of uric acid. Before therapeutics can make much advance in this direction we must know more about the pathology of gout and tissue metabolism generally, and we may then hope that not only will people be more free from the manifold symptoms that gout produces, but will live longer, and the time of their activity, bodily and mental, will continue nearly as long as life itself. The power of increasing elimination of nitrogenous waste which urea possesses in a marked degree is shared by other substances belonging to the so-called purin group, and day by day fresh bodies belonging to this chemical group are being made synthetically. Some of the new ones seem to have a greater power of eliminating waste than any we have hitherto had. The observations of Richardson that alcohols vary in their action according to their chemical composition, and of Crum, Brown and Fraser that alteration in chemical constitution brought about change in physiological action, are now beginning to bear rich fruit, and the synthetic preparation of remedies having different pharmacological properties along with our increasing knowledge o pathology, gives us much hope for the future of therapeutics. More than two hundred years ago Locke said if we knew the effect of drugs on man as a watchmaker does those of his operations on a watch, we should know that aloes would purge, hemlock would kill, and opium make a man sleep. One of the grea problems of therapeutics is not only to know what drugs to use in order to obtain certain effects, but to know how to make such drugs if we have not got them at hand.

The struggle for existence does not occur only between man and beast, man and man, nation and nation, nor even between individual beasts or plants. It takes plac also between cell and cell, not only between those cells which we term microbe and the cells of which the human bod consists, but even between those whic form the different parts of the body itsel The great object of this congress is t unify knowledge, to render evident th similarity of the laws which gover phenomena of the most diverse characte and it is therefore interesting to find tha the grand problem of therapeutics is fo the cell what those of religion and soc ology are for the man, viz., to learn ho to regulate the environment of each ma or cell in such a manner that the ind vidual shall not work for his or its ow good alone, but for that of others as wel and that useless or noxious individua shall be repressed or destroyed.

When we are able to regulate cell li by food, air, water, exercise, inoculatio or medicines, we shall be able to relieve o remove weakness, pain or distress n only from the bodies but also from th minds of our patients, to maintain healt increase strength, and prolong life to a extent of which at present we can hard dream.

TIGHT

GUTTERS.